Exhibit B

GENERAL TVT & TVT-O EXPERT REPORT OF DENISE M. ELSER, M.D.

Introduction

I am board-certified in Female Pelvic Medicine and Reconstructive Surgery (commonly known as Urogynecology), as of June 2013, the first time the board certification in FPMRS was offered. I am the Medical Director of Women's Health Institute of Illinois, a busy private practice in the suburbs of Chicago.

I have been performing incontinence surgeries initially as a resident physician, during my urogynecology fellowship and as an attending urogynecologist since 1995. I have performed many different types of procedures to treat stress incontinence: anterior repairs, open and laparoscopic retropubic urethropexies including Burch and Marshall-Marchetti-Krantz (MMK) procedures, needle suspensions, fascial bladder neck slings, injection of periurethral bulking agents, transurethral collagen denaturation (formerly Renessa®, now known as Lyrette®), and synthetic mid-urethral slings. I have performed a variety of surgeries for treatment of pelvic organ prolapse. These include anterior and posterior colporrhaphy, native tissue vault suspension (Sacrospinous ligament fixation and uterosacral suspension), vaginal repair with mesh augmentation, and abdominal sacrocolpopexy- both open and robotically.

I have performed approximately 2,000 synthetic midurethral slings since 1998, averaging about 100-150 slings per year. This includes retropubic, obturator and single incision sling approaches. I first began using the TVT in approximately 1998, and began using TVT-O in 2005. I have also used the TVT Abbrevo and TVT Exact devices. I am currently involved in teaching residents and previously fellows. I have served as a preceptor for both Ethicon and

Boston Scientific in cadaver labs, and as a preceptor in the Operating Room, teaching slings and vaginal mesh procedures to other physicians. In a typical week, I perform numerous incontinence and prolapse surgeries involving mesh and native tissue repairs, in addition to other surgeries. I have also performed revision surgeries following incontinence and prolapse surgeries. Our practice's sling revision rate for either exposure or incomplete bladder emptying is 4.5%.

My curriculum vitae is enclosed and it provides additional information regarding my background, qualifications and publications. (Attachment A). Materials that I have reviewed are cited in this report and attached along with materials which I may use at trial. (Attachment B). All of my opinions are held to a reasonable degree of medical and scientific certainty. I reserve the right to amend and provide additional opinions as additional information becomes available and following the depositions of the experts for Plaintiffs.

Testimonial history

In the past 4 years, I have been deposed as an expert in Edward versus Ethicon, MDL April 24, 2014, Bellew versus Ethicon, MDL September 16, 2014, Budke versus Ethicon, Missouri November 6, 2014, and Corbet versus Ethicon, NJ November 5, 2015. I gave trial testimony in Carlino versus Ethicon, Pennsylvania CCP on February 4-5, 8, 2016.

OPINIONS

Urinary Incontinence

Urinary incontinence or the involuntary leakage of urine affects women of all ages. The reported incidence varies depending on the study, and may vary depending on population studied, method of recording leaks and the definition of leakage used by the authors. Currently, best estimates are that accidental leakage of urine affects 10-55% of women on a regular basis.

One way to define type of accidental urine leakage is by using patient symptoms. The following are symptom-based definitions:

- Stress urinary incontinence (SUI) refers to accidental leakage of urine which occurs with physical stress on the bladder, as occurs with coughing, sneezing, jumping, standing, or lifting a heavy object. In extreme cases, stress leakage can occur simply as a result of a change in position, or can even become continuous.

- Urge urinary incontinence (UUI) refers to sudden leakage, usually of large amounts of urine, preceded by a warning, or an urge to urinate. Women with mixed incontinence experience symptoms of both stress incontinence and urge incontinence.

- Overactive Bladder (OAB) refers to a constellation of symptoms including urgency, frequency, urge incontinence, and nocturia (the need to pass urine at night).

Urodynamics testing is used to document bladder function. Some generally-accepted definitions of urinary incontinence are published by the International Continence Society. The most recent publication came about after the 2009 International Consultation on Incontinence. Urodynamic stress incontinence (USI) is noted during filling cystometry and is defined as the involuntary leakage of urine during increased abdominal pressure, in the absence of a detrusor contraction. An older term for USI is Genuine Stress Incontinence (GSI). Idiopathic Detrusor Overactivity (IDO) is defined as overactivity when there is no clear cause. Neurogenic Detrusor Overactivity (NDO) is defined as overactivity due to a relevant neurological condition. An older term for this condition is Detrusor Instability.

In general terms, women with SUI have a combination of weak ligament support and weak pelvic muscles. Other factors are increased abdominal pressure, such as occurs with chronic cough and obesity; or inherently weak periurethral tissues or a loss of elasticity of the urethra so that there is not coaptation of the urethral walls. A more severe form of SUI is known as Intrinsic Sphincteric Deficiency (ISD). ISD is defined as Low Leak Point Pressure as measured on urodynamics testing, most commonly under 60 cmH2O. Drainpipe urethra implies a urethral lumen that does not close, even at rest, with lack of hypermobility of the urethra. Hypermobility or an excursion of the urethral angle greater than 30 degrees with strain or cough implies weak ligamentous support of the urethra.

Known risk factors for stress urinary incontinence include: age, pregnancy/childbirth, obesity, genetic predisposition/ethnic heritage, menopausal status, diabetes, kidney disease, smoking, chronic coughing and other factors. (KML) Stress incontinence can have a

significantly negative effect on quality of life. Incontinent women score more poorly on Quality of Life (QOL) standardized questionnaires. Between 25 and 50% of incontinent women experience sexual dysfunction. Incontinence is associated with depression. Up to 23% of women miss work due to incontinence.

Options for treating SUI include behavioral treatments, non-surgical treatments and surgical procedures. Behavioral methods include weight loss, control of chronic cough, decreasing fluid intake, and timed voiding. Non-surgical treatments include pelvic muscle (Kegel) exercises, with or without the aid of a pelvic floor physical therapist, biofeedback devices or intravaginal electrical stimulation, an intravaginal incontinence pessary (a device worn in the vagina that externally compresses the urethra), urethral caps (Capsure®), urethral inserts (Femsoft®) and possibly timed voiding. I do not routinely offer biofeedback devices, electrical stimulation, urethral caps or urethral inserts. In my experience, urethral caps and inserts are not tolerated by the vast majority of women. A new product, Poise® Impressa® Bladder Supports (Kimberly Clark) was released this year as a vaginal tampon to be worn intending to create a transient urethral obstruction by placing pressure on the urethra. Women wear the device when they want to avoid leakage, and remove the disposable device in order to urinate. Impressa® is intended as an alternate to pads, avoiding wetness on the perineum, but will not correct urinary incontinence. Manual physical therapy with an experienced pelvic floor physical therapist is far more effective than use of biofeedback devices and/ or a home electrical stimulation program. Procedures or surgeries to treat SUI include injection of periurethral bulking agents, sling surgery, or abdominal retropubic urethropexy. Bulking agents are indicated for patients with ISD. I will occasionally use injections on frail elderly women even

if ISD has not been demonstrated by urodynamics testing. These injections are performed only in rare exceptions on young, healthy women. Injections currently available in the US include autologous fat, bovine collagen (Contigen®; Bard Urological), calcium hydroxylapatite (Coaptite®; Bioform Medical, Inc.), carbon beads (Durasphere®; Coloplast Corp.), polydimethylsiloxane (Macroplastique®; Uroplasty, Inc.), and ethylene vinyl alcohol (EVOH) copolymer suspended in dimethyl sulfoxide (Tegress®; C. R. Bard, Inc.). Tegress and Contigen are no longer sold in the United States. Injection of autologously-harvested stem cells is currently under investigation. Radiofrequency collagen denaturation, once sold as Renessa®, and now marketed as Lyrette®, is an office-based procedure performed under local anesthesia with or without sedation used to treat urinary incontinence. The procedure was cleared for marketing by the FDA in 2005. I have authored studies on this device for treatment of SUI. I no longer offer this treatment, mainly due to lack of third party coverage in Illinois.

Brief history of development of surgeries for SUI

Surgical options include anterior colporrhaphy (anterior repair), pubovesical sling using autologous fascia, cadaveric human fascia or dura mater, other biologics, synthetic midurethral sling, and retropubic urethropexy (Burch or MMK). Pubovesical slings are also known as pubovaginal slings or bladder neck slings. The evolution of surgical treatments of stress incontinence has occurred over the 2 decades that I have been practicing.

In the 1980s, anterior repair was commonly performed as a treatment not only for correction of prolapse, but also for stress incontinence. Retropubic urethropexies, in the form of Burch or MMK procedures were also performed but were not in the skill set of most

Urologists or Gynecologists. The field of Urogynecology was in its very early stages during this period. A variety of needle suspensions came into play very quickly during this time period, as easy-to-learn, minimally- invasive cures for stress incontinence. One landmark study helped to convince surgeons that anterior repair and needle suspensions ought not to be considered as primary treatment for GSI, as it was known as the time. Bergman and colleagues randomized women with incontinence to undergo one of 3 procedures: 1) anterior colporrhaphy with Kelly plication; 2) modified Pereyra needle urethropexy, and; 3) Burch urethropexy. The objective success rates for groups 1, 2 and 3 after 5 years were 37%, 43%, and 82%. Burch became the gold standard surgery for GSI. (Bergman et al)

Incontinence surgeons were still looking for a minimally-invasive surgical treatment for stress incontinence. Pubovesical slings were placed at the bladder neck, not the midurethra as modern synthetic slings are positioned. Because of the high rate of complications, including permanent irritative voiding symptoms or permanent complete retention of urine, these slings were initially reserved for women with severe stress debilitating stress incontinence, ISD, typically after failed alternate procedures. Women were generally counseled that the risk of urinary retention requiring Clean Intermittent Straight Catheterization, (CISC) was about 15-20%. However, even women who agreed to this procedure understanding the risks tended to become unhappy after several months of catheterizing themselves several times per day. Therefore, many articles appeared in the medical literature in the 1990s regarding urethrolysis, or an attempt to surgically restore mobility to the urethra after a sling or Burch resulted in retention.

An article co-authored by Dr. Blaivas described a suprameatal approach to urethrolysis after several different types of incontinence surgeries. (Petrou 1999) However, urethrolysis after Burch or bladder neck sling did not necessarily restore voiding problems or reduce irritative symptoms. Weinberger et al reported on 108 women undergoing polytetrafluoroethylene (Gore-Tex) suburethral sling and concluded that this sling commonly produces permanent voiding dysfunction. Further, they commented that sling removal does not ensure resolution of urinary retention. (Weinberger MW et al).

Even a rather recent article reported on voiding dysfunction after Burch and pubovaginal slings. (Lemack GL et al) This multicenter group compared outcomes with pubovaginal sling using fascia with Burch urethropexy. The study defined voiding dysfunction as use of any bladder catheter after 6 weeks or reoperation for takedown of sling or Burch. Voiding dysfunction developed in 57/655 (9%) women; 8 in the Burch group and 49 in the pubovaginal sling group. The authors did not report whether or not sling takedown resolved the voiding complaints. In 2001, Richter HE et al reported on a series of women undergoing a variety of fascial slings. They reported that almost 12% of subjects required regular self-catheterization post- operatively. Another prospective trial comparing Burch to the Lyodura sling reported late post-operative voiding dysfunction in 29% of women post-sling and 10% post-Burch. Eighty-three percent (5/6) experienced new-onset detrusor instability. (Ostergard 1997)

While some groups worked on performing Burch procedure laparoscopically, others sought an alternative to autologous fascia for sling procedures. Autologous slings used fascia

harvested from a patient's abdominal wall, the rectus sheath, or fascia lata, harvested from the thigh. Rectus fascia was of questionable quality. In women with a history of pregnancy, the fascia may have stretched or torn. (It should be noted that incontinence is associated with a genetic predisposition to weaker collagen tissue.) Harvesting fascia lata from the thigh involved a thigh incision and rotation of an anesthetized patient after the harvest. This increased pain, risk, cost, and length of surgery. Kaplan et al reported on complications related to autologous harvest of fascia lata. (Kaplan SA 1996) My group at Medical College of Virginia was likely the first in the US to use banked donor material (dura) for bladder neck slings in the years 1992-1995. Soon after, Handa reported on 16 women who underwent suburethral sling using allogenic fascia (human cadaver donor). Twelve percent (12%) developed abdominal wound infections. Mean duration of bladder drainage was 29 days. One patient (6%) continued CISC at 187 days. Objective cure rate was 79%.

Other surgeons explored implantation of synthetic material for bladder neck slings. Adverse events following implantation of strips of Gore-Tex and Marlex prevented widespread adoption of these materials. (Morgan 1985)

Dissatisfied with results of anterior repair and needle suspension, with the recovery associated with Burch, and with the voiding dysfunction associated with slings, a relatively small group of urogynecologists began exploring laparoscopic Burch. The procedure involved suturing deep in the pelvis, requiring technical skills that are not available to many surgeons. In 2000, results of a long-awaited multicenter trial of Urogynecologists who with excellent laparoscopic skills were published. (Summitt RL et al). Sixty-two women were randomly assigned to receive

laparoscopic or transabdominal Burch. The authors reported that while there were differences in operating time and length of hospital stay, the results were not significantly different. Because of concerns about costs, length of surgery and lack of reproducibility in other surgeons' hands, laparoscopic Burch was not widely adopted.

SISTEr Study

An important study was published by the UITN (Urinary Incontinence Treatment Network), the SISTEr trial. (Albo NEJM 2007). The abstract for the SISTEr study provides, in pertinent part, that it was a:

> Multicenter, randomized clinical trial comparing two procedures the pubovaginal sling, using autologous rectus fascia, and the Burch colposuspension in women with stress incontinence... The primary outcomes were success in terms of overall urinary-incontinence measures, which required a negative pad test, no urinary incontinence (as recorded in a 3-day diary), a negative cough and Valsalva stress test, no self-reported symptoms, and no retreatment for the condition, and success in terms of measures of stress incontinence specifically, which required only the latter three criteria... A total of 655 women were randomly assigned to study groups: 326 to undergo the sling procedure and 329 to undergo the Burch procedure; 520 women (79%) completed the outcome assessment.
>
> At 24 months, success rates were higher for women who underwent the sling procedure than for those who underwent the Burch procedure, for both the overall category of

success (47% vs. 38%, P = 0.01) and the category specific to stress incontinence (66% vs. 49%, P<0.001).

However, success came at the cost of more complications. According to the SISTEr study, "surgical procedures to reduce voiding symptoms or improve urinary retention were performed exclusively in the sling group, in which 19 patients underwent 20 such procedures." Additionally, "[a]t the time of hospital discharge, fewer patients in the sling group than in the Burch group had voiding with a residual volume of less than 100 ml (44% vs. 58%), and the difference persisted at 6 weeks (86% vs. 97%)."

The SISTEr study defined voiding dysfunction as "the need for surgical revision to facilitate bladder emptying or the use of any type of catheter after the 6-week visit." Under this definition, "[v]oiding dysfunction was more common in the sling group than in the Burch group (14% vs. 2%, P<0.001). More patients were treated for postoperative urge incontinence in the sling group than in the Burch group (87 patients [27%] vs. 65 patients [20%], P = 0.04)." The authors noted that the rate of postoperative urge incontinence was likely underestimated as the definition was "restricted to patients who received treatment for this condition."

Results indicated that "[a]dverse events were more common in the sling group than in the Burch group (63% vs. 47%, P<0.001), with 415 events among 206 women in the sling group, as compared with 305 events among 156 women in the Burch group." Both groups had a significant number of urinary tract infections; "157 women in the sling group (48%) had 305 events and 105 women in the Burch group (32%) had 203 events."

Wound complications requiring surgical intervention totaled 12 in the Burch and 11 in the Fascial sling: incisional hernia (Burch, 5 patients; sling, 3), seroma or hematoma (Burch, 2; sling, 3), infection (Burch, 2; sling, 2), abscess (Burch, 1; sling, 1), and vaginal wound revision (Burch, 3; sling, 2). Wound complications not requiring surgical intervention totaled 69 in the Burch and 71 for fascial sling: 2 sling exposures (visualization of the sling material in the vagina), incisional hernia (Burch group, 2; sling group, 1), superficial wound-edge separation (Burch, 10; sling, 5), seroma or hematoma (Burch, 13; sling, 11), infection (Burch, 31; sling, 21), and granulation tissue or stitch granulomas (Burch, 13; sling, 31).

More recently, longer term data from the SISTEr trial were published. Continence rates at 5 years were Burch 24.1% versus Fascial sling 30.8% (p=0.002 in favor of Fascial sling). (Brubaker 2012 J. Urology). At 7 years, continence rates had continued to significantly decrease to Burch 13% and Fascial sling 27%. (Richter 2012 J. Urology).

Introduction of the synthetic Mid-urethral sling

Papa Petros and Ulmsten published their "Integral Theory" in a Scandinavian journal in 1990. Further work suggested that providing support at the midurethra rather than the bladder neck would restore anatomy and continence. (Petros PP 1990). Ulmsten presented his data on using a synthetic midurethral sling under local anesthesia as an outpatient procedure in 1996 (Ulmsten 1996). The tension free vaginal tape (TVT) manufactured by Ethicon received FDA clearance in 1998. Since that time, over 3 million TVT slings have been implanted in women for treatment of SUI. (AUGS/SUFU Position Statement 2014) The procedure became widely

adopted because it was minimally invasive, had reproducible good results and had a good safety record.

Ward and Hilton led a multicenter trial in the United Kingdom (UK) and Ireland comparing 344 women randomized to TVT or Burch for primary SUI. The initial two-year data led many to consider TVT a superior approach. They found no significant difference in cure for GSI, but more women in the Burch group had wound complications, more permanent urinary retention requiring CISC and more surgery for uterovaginal prolapse in the 2 years post-op. (Ward KL 2004) The concept that a Burch urethropexy also known as a Burch colposuspension predisposed to or caused prolapse in women. More than a decade earlier, Stuart Stanton's group reported on 131 patients who underwent Burch performed by Dr. Stanton between 1977-1986. Twenty-Six percent (35/131) women required 40 operations to correct symptomatic pelvic organ prolapse after undergoing a Burch. The outcomes were not affected by age, parity, menopausal status or prior pelvic surgery. The authors concluded that this apparently increased of prolapse may be due to creation of an abnormal vaginal axis or by intrinsic tissue weakness. (Wiskind AK 1992)

In 2008, the same group published the 5 year data on these women, which firmly established TVT as the gold standard surgical treatment for women with SUI. In this study, 170 women underwent TVT and 146 underwent Colposuspension. The authors concluded that TVT is as effective as Burch for treatment of SUI, with effect on cure of incontinence, improvements in quality of life and sexual health maintained at 5 years after surgery. (Ward 2008)

The obturator technique for synthetic midurethral sling placement was introduced by DeLorme with an "outside-in" approach, and later DeLeval for the "inside-out" approach. (DeLorme2004) (DeLeval 2003) De Leval's technique evolved into the Ethicon TVT-O sling, which was introduced to the US marketplace in 2004.

Obturator slings became popular quickly because they appeared to decrease chance of bladder injury during the procedure and did not *require* cystoscopy. Early reports questioned efficacy of retropubic versus obturator in cases of pure SUI or mixed incontinence (urge and stress symptoms). A recent review by Cox et al found that:

> Both retropubic and transobturator midurethral slings are effective for patients with mixed urinary incontinence, but the overall cure rate is lower than for patients with pure SUI. Based on the literature a new gold standard first-line surgical treatment for women with SUI is the synthetic midurethral sling inserted through a retropubic or transobturator approach. (Cox et al 2013)

TOMUS Trial

The UITN also conducted the ToMUS trial, which compared MUS – specifically the TVT to the TVT-O and TOT, and similar to SISTEr data are available at 24 months. (Albo 2012 J. Urology). In this multicenter controlled trial, 597 stress incontinent women were randomized to TVT retropubic versus TVTO or TOT. The primary outcomes were objective (negative stress test, negative pad test and no re-treatment" for stress urinary incontinence) and subjective (no self-report of stress urinary incontinence symptoms, no leakage episodes on 3-day bladder diary and no re-treatment for stress urinary incontinence) success at 24 months. Objective

success rates for retropubic and transobturator mid urethral slings were 77.3% and 72.3%, respectively and subjective success rates were 55.7% and 48.3%, respectively. The rates of patient satisfaction with the treatment were similar between the retropubic-sling group and the transobturator-sling group (85.9% and 90%, respectively; P=0.14). Neither objective nor subjective success rates met the prespecified criteria for equivalence. Frequency of de novo urgency incontinence (retropubic 0% vs transobturator 0.3%, p = 0.99) were similar in both groups. The retropubic mid urethral sling group had higher rates of voiding dysfunction requiring surgery (2.7% vs 0%, p = 0.002) and urinary tract infections (17.1% vs 10.7%, p = 0.025). The frequency of neurologic symptoms was also higher in the transobturator-sling group than in the retropubic-sling group (P=0.01); weakness in the upper leg was the most common neurologic symptom. There were 11 wound complications in each arm requiring surgical intervention, the majority of which were mesh exposures.

In my opinion, mesh exposures can often be conservatively managed. When surgery is warranted, these are usually short, outpatient procedures, which do not necessarily require general anesthesia, and often do not require an incision. Wound complications not requiring surgical intervention totaled 6 in the TVT arm and 2 in the TOT arm, and again the majority were mesh exposures. The occurrence of mesh exposure (retropubic 4.4% vs transobturator 2. 7%, p = 0.26) was not significantly different. When one compares the wound complications occurring in the SISTEr and ToMUS trials it is apparent that there are more wound complications with the Burch and facial sling.

Kobashi and Govier reported on vaginal mesh exposures after sling surgery, specifically the SPARC (American Medical Systems), a type of retropubic midurethral sling. In their initial series of 90 patients, 4 were found to develop mesh exposure post operatively. In two patients, the exposure was completely asymptomatic and found incidentally during exam. The other 2 patients experienced a vaginal discharge, and 1 complained of partner discomfort during intercourse. All 4 were treated conservatively, and all resolved spontaneously with no negative sequelae. (Kobashi 2003)

Hematomas are a known complication of any surgery let alone pelvic surgery with or without use of trocars or mesh. These risks are well known to surgeons performing stress incontinence and prolapse repairs. Drs. Kuuva and Nilsson reported on the national database acquired in Finland through the end of calendar year 1999. (Kuuva 2002) There were 38 hospitals reporting on 1,455 slings. The incidence of retropubic hematoma was 19/1000. In another study, co-authored by Nilsson, Kuuva and others, the 5 year results of retropubic TVT's in 90 consecutive patients from a Nordic multicenter study were reported. While 85% of women were both objectively and subjectively cured, another 10.6% were significantly improved. The incidence of post-op retropubic hematoma was 3.3% in this series.

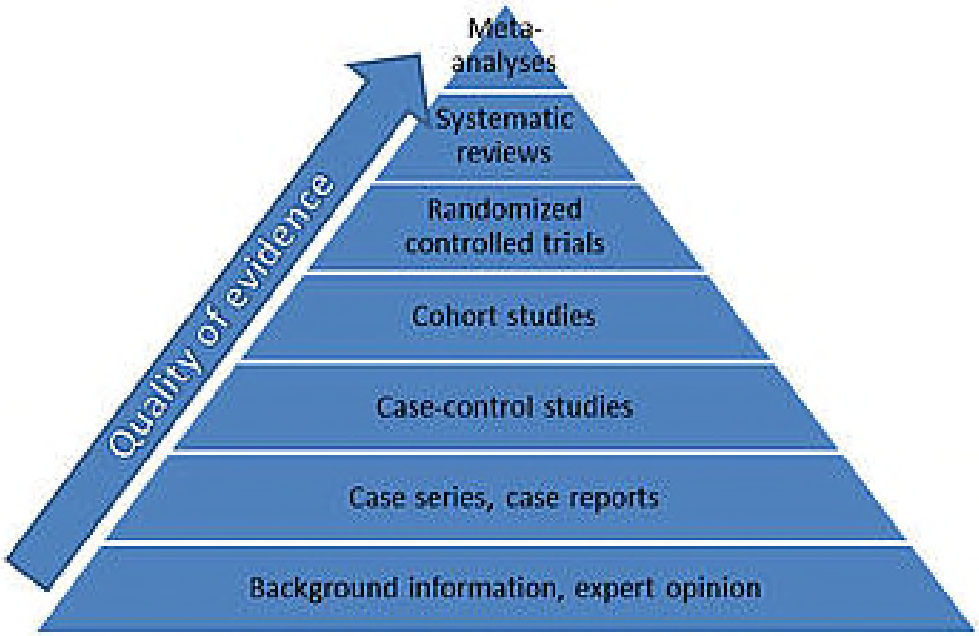
In 2007, LaSala reported on 2 patients with retropubic hematomas in the space of Retzius after the use of mesh kits for prolapse. The hematomas were 6.5 – 7 cm in diameter. Drainage was not required in either case, but resolution was completed by 6 months postoperatively. Kobashi reported on her experience tracked over the first 140 midurethral slings. One woman out of 140 developed a retropubic hematoma that required percutaneous

drainage. (Kobashi 2003) Earlier, in 2003, Karram reported on his 350 midurethral slings. 6 patients developed retropubic hematomas. Two-thirds of these were asymptomatic. All hematomas resolved spontaneously. (Karram 2003)

Hematomas are not limited to retropubic midurethral slings. In 1994, Colombo published a randomized controlled trial (RCT) comparing Burch to Marshall-Marchetti-Krantz (MMK) Procedure. Eighty women were included in this study. Two women in the MMK developed large retropubic hematomas; one requiring transfusion. The TVT IFU adequately warns of the risk of hematoma by warning of punctures or lacerations to vessels. (TVT IFU.)

Cochrane Reviews

There are several Cochrane reviews which support the TVT and TVT-O devices and the data show that these devices are safe and effective. Cochrane reviews are of the highest level of evidence as demonstrated by the Oxford Levels of Evidence pyramid:



http://www.cebi.ox.ac.uk/for-practitioners/what-is-good-evidence.html

Minimally invasive MUS including TVT and TVT-O were the subject of a Cochrane Review by Ogah. (2009). Per the abstract, results were as follows:

> "Sixty-two trials involving 7,101 women were included. The quality of evidence was moderate for most trials. Minimally invasive synthetic suburethral sling operations appeared to be as effective as traditional suburethral slings [8 trials, n=599, risk ratio (RR) 1.03, 95% confidence interval (CI) 0.94--1.13] but with shorter operating time and less postoperative voiding dysfunction and de novo urgency symptoms. Minimally invasive synthetic suburethral sling operations appeared to be as effective as open retropubic colposuspension (subjective cure rate at 12 months RR 0.96, 95% CI: 0.90--1.03; at 5 years RR 0.91, 95% CI: 0.74--1.12) with fewer perioperative complications, less

postoperative voiding dysfunction, shorter operative time, and hospital stay but significantly more bladder perforations (6% vs. 1%, RR 4.24, 95% CI: 1.71--10.52). There was conflicting evidence about the effectiveness of minimally invasive synthetic suburethral sling operations compared to laparoscopic colposuspension in the short term (objective cure, RR 1.15, 95% CI: 1.06--1.24; subjective cure RR 1.11, 95% CI: 0.99--1.24). Minimally invasive synthetic suburethral sling operations had significantly less de novo urgency and urgency incontinence, shorter operating time, hospital stay, and time to return to daily activities. A retropubic bottom-to-top route was more effective than top-to-bottom route (RR 1.10, 95% CI: 1.01--1.20; RR 1.06, 95% CI: 1.01--1.11) and incurred significantly less voiding dysfunction, bladder perforations, and tape erosions. Monofilament tapes had significantly higher objective cure rates (RR 1.15, 95% CI: 1.02--1.30) compared to multifilament tapes and fewer tape erosions (1.3% vs. 6% RR 0.25, 95% CI: 0.06--1.00). The obturator route was less favorable than the retropubic route in objective cure (84% vs. 88%; RR 0.96, 95% CI: 0.93--0.99; 17 trials, n=2,434), although there was no difference in subjective cure rates. However, there was less voiding dysfunction, blood loss, bladder perforation (0.3% vs. 5.5%, RR 0.14, 95% CI: 0.07--0.26), and shorter operating time with the obturator route."

Several other Cochrane Review and meta-analyses have been performed which show a beneficial benefit to risk profile and these data also show that TVT and TVT-O are less invasive than the Burch and Fascial slings. (Cox 2013 Nat Rev Urol).

Most recently, an updated Cochrane review (Ford 2015) assessed the literature including RCTs and registries and observed that for TVT the number of procedures reported ranged from 809 to 4281, and there were found to be low rates of major complications:

- Bladder perforation occurred in 2.7% to 3.9% of cases.
- Reoperation rates relating to tape insertion or postoperative voiding dysfunction (POVD) ranged from 1.6% to 2.4%.
- Urinary retention rate was 1.6%.
- Pelvic hematoma occurred in 0.7% to 1.9% of women.
- Infection rate was 0.7%.
- Vaginal tape erosion/extrusion rate was 1.5%.
- Groin pain occurred in 0.4% of women.

The authors noted that these rates were reflective of those reported in the trials included in the Cochrane review. There were also few cases of major visceral injuries such as bowel and urethral injuries.

Registries of transobturator tapes including TVT-O had low rates of complications as well:

- Bladder perforation occurred in 0.4% of cases.
- Reoperation rates relating to tape insertion ranged from 0.8% to 2.2%.
- Urinary retention rate was 0.5%.
- Pelvic hematoma occurred in 0.5% of women.
- Infection rate was 0.6%.

- Vaginal tape erosion/extrusion rate was 0.4%.
- Groin pain occurred in 1.6% of women.

Overall, these registries whose primary focus was assessment of complication rates are consistent with the randomized controlled trials and longer term data on TVT and TVT-O and demonstrate their safety and efficacy.

The systematic reviews, metaanalyses, and assessment of high level data by Cochrane and others renders the low level data and irrelevant materials cited by Plaintiffs' experts obsolete and demonstrates their lack of methodology. The TVT and TVT-O studies report low rates of exposure (2%), chronic pain and dyspareunia, and the Ford 2015 Cochrane Review concluded that mid-urethral sling operations, and in particular the TVT and TVT-O which have the most data, "have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI." They also concluded that the "reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of these tapes." I share in these opinions based on these and other data as set forth in this General Report.

Official guidelines from governmental agencies or medical societies regarding SUI surgery and slings

American Urogynecologic Society and Society of Urodynamics and Female Urology

In January 2014, the American Urogynecologic Society (AUGS) and the Society of Urodynamics and Female Urology (SUFU) released a joint position statement strongly advocating the use of synthetic midurethral slings in the treatment of Stress Urinary Incontinence in women. The key points of the statement are:

1. Polypropylene material is safe and effective as a surgical implant.
2. The monofilament polypropylene mesh MUS is the most extensively studied anti-incontinence procedure in history.
3. Polypropylene mesh midurethral slings are the standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients.
4. The FDA has clearly stated that the polypropylene MUS is safe and effective in the treatment of SUI.

The statement concludes that this procedure (MUS) is “the most important advancement in the treatment of SUI in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence.” I am a member of AUGS and I am in agreement with the statement.

On Mar. 26, 2013 AUGS published their "Position Statement on Restrictions of Surgical Options for Pelvic Floor Disorders". I agree with their conclusions:

- "“Any restriction of mesh slings for the treatment of stress urinary incontinence is clearly not supported by any professional organization or the FDA.”

- "Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard of care for stress incontinence surgery."

- "In a recent study involving 53 expert urologists and Urogynecologists (of whom >90% were fellowship trained) and who could select among many surgical options, the full-length synthetic midurethral sling was the preferred option in 93% for the surgical treatment of primary stress incontinence.""

On March 12, 2014, AUGS and SUFU released Frequently Asked Question (FAQ) documents for patient and providers on mesh midurethral slings for SUI. Some of the significant commentary in the provider FAQ's include that "currently available mid-urethral slings are composed of macroporous, knitted, monofilament polypropylene, sometimes known as "Type I" meshes… As an implant for the surgical treatment of SUI, macroporous, monofilament polypropylene has demonstrated long-term durability, safety, and efficacy for up to 17 years. In response to the question: "Does the MUS mesh made of polypropylene degrade over time? ", the response is "Polypropylene is a stable and well-accepted biomaterial with a history of over five decades of use in mesh implants. In recent years, concerns regarding implanted polypropylene degradation have been raised as a result of very high-magnification images that show portions of some explanted synthetic meshes with "cracked" surfaces. These surface changes were further hypothesized to lead to adverse clinical outcomes, though this is not supported by the extensive peer-reviewed literature related to polypropylene mesh repairs.

Prospective studies have followed patients with implanted mid-urethral slings for 17 years and show excellent durability and safety of the procedure." My analysis of the literature also leads me to the same conclusion. I am aware that the experts for the plaintiff also claim that the mesh is cytotoxic or can cause sarcomas and cancer. Like the claim of degradation, I do not believe that the clinical literature supports these claims and I have not seen evidence of degradation, cytotoxicity, malignant transformation or cancer in my clinical practice.

International Continence Society (ICS)

ICS Fact Sheets: A Background to Urinary and Faecal Incontinence issued July 2013 concluded that:

- "Worldwide, midurethral slings compromised of synthetic mesh have become the treatment of choice for SUI. Long-term data are robust and demonstrate durable efficacy with a very low complication rate, particularly in experienced hands."
- "The long-term complications of surgical mesh sling repair for SUI that are reported in the literature are consistent with the adverse events reported to the FDA."

AUA (American Urological Association)

"AUA Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence" from October 2013. This statement concludes that:

- "Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries."

- "Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries and are known to occur with non-mesh sling operations as well."

- "It is the AUA's opinion that any restriction on the use of synthetic polypropylene mesh suburethral slings would be a disservice to women who choose surgical correction of SUI.""

The 2009 AUA's Guideline Update on the Surgical Management on the Surgical Treatment of Female Stress Urinary Incontinence evaluated the different surgical treatment options and recognizes midurethral slings like TVT as a first line treatment option. This update shows operative and subjective complications for "Slings – Synthetic at Midurethra" without prolapse as having pain at 1%, sexual dysfunction at 0%, and voiding dysfunction at 2%. Meanwhile, "Autologous Fascia" slings without Bone Anchors shows pain at 10% and sexual dysfunction at 8%, as well as reporting the Burch procedure with pain at 6%, sexual dysfunction at 3%, and voiding dysfunction at 10%. The AUA updated these guidelines in October 2013, and

now attest that multiple publications including case series and RCTs attest to the long term efficacy (5-10 years) of synthetic midurethral slings. Further there is "no significant increase in adverse events observed over this period of follow-up". Finally, they confirm that synthetic slings are not only an "appropriate" surgical choice for the surgical treatment of USI but that they offer "less morbidity that conventional non-mesh sling techniques." (AUA position statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence)

American College of Obstetrics and Gynecology (ACOG) Practice Bulletin

The American College of Obstetricians and Gynecologists (ACOG) and the American Urogynecologic Society (AUGS) have recently co-produced a new Practice Bulletin titled: "Urinary Incontinence in Women." (ACOG Number 155- November 2015). Practice Bulletins are reliable sources of information and inform surgeons about current information on techniques, clinical management issues and provide recommendations based on current medical evidence. This documents states that "most of the chronic complications related to Burch colposuspension and sling procedures relate to voiding dysfunction and urge symptoms" (ACOG Nov 2015). Further, the authors state that synthetic midurethral synthetic mesh slings have become the primary surgical treatment for stress urinary incontinence because of reasons related to efficacy, adverse events are lower than that for suburethral fascial slings, and less voiding dysfunction than for open colposuspension. The ACOG Practice Bulletin establishes that the TVT and TVT-O are safe and effective, suitable first line surgical options for the treatment of SUI.

Food and Drug Administration (FDA)

The FDA concluded in their "Considerations about Surgical Mesh for SUI" dated March 27, 2013 that: “The safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year.”

NICE Guidelines

The following is taken from the NICE guidelines website as of March 2014. The National Institute for Health and Care Excellence aka NICE produces guidelines that govern their health care system. According to the website, “the quality standards are a concise set of prioritized statements designed to drive measurable quality improvements within a particular area of health or care.” These guidelines are at times more advanced and more stringent than US guidelines and incorporate evidence based practice as well as cost effective measures.

When offering a synthetic mid-urethral tape procedure, surgeons should:

- use procedures and devices for which there is current high quality evidence of efficacy and safety
- use a device manufactured from type 1 macroporous polypropylene tape
- Consider using a tape colored for high visibility, for ease of insertion and revision.

- Not offer anterior colporrhaphy, needle suspensions, paravaginal defect repair and the Marshall–Marchetti–Krantz procedure for the treatment of stress UI.

Further, "Use procedures and devices for which there is currently high quality evidence of efficacy and safety [footnote 11 further concludes that "The guideline only recommends the use of tapes with proven efficacy based on robust RCT evidence…. At the time of publication (September 2013) the following met the Guideline Development Group criteria: TVT or Advantage for a 'bottom-up' retropubic approach; TVT-O for an 'inside-out' transobturator approach…"].

The British Association of Urological Surgeons (BAUS) in their "Synthetic Vaginal Tapes for Stress Incontinence" dated December 2012 as follows:

- "The TVT & TOT are now the most commonly performed operations for stress incontinence in the UK. Both procedures are relatively quick, taking around 30 minutes to perform, either under general or local anesthesia. The operations are performed as a day case, meaning that you can go home on the same day." "The overall success can also be expressed as a satisfaction rate and approximately 9 out of 10 women are satisfied with the result after either a TVT or a TOT."

- "The previous most common operation that was done for stress incontinence is called the Burch colposuspension. However, this is a much more invasive procedure and involves making a cut in the lower abdomen, above the pubic bone, in order to support the neck of the bladder."

<u>European Association of Urology (EAU)</u>

EAU Guidelines on Surgical Treatment of Urinary Incontinence were issued September 17, 2012. These guidelines conclude that "There has been a rapid adoption of midurethral synthetic sling insertion as the first-line surgical option for SUI because it is effective, it is less invasive, and patients recover more quickly." EAU recommends the MUS as a first line surgical option.

Society of Gynecologic Surgeons (SGS)

The recent systematic review and meta-analysis by SGS evaluated the literature regarding surgical treatment of SUI and recommended MUS like TVT and TVT-O as a suitable first line surgical option as compared to Pubovaginal slings and Burch urethropexies. No significance in effectiveness between retropubic and obturator MUS were found. (Schimpf 2014) Complications for the various procedures were analyzed and in my opinion, complications with the TVT and TVT-O compared favorably with the other procedures. Dyspareunia was noted as rare.

Guidance from Medical Education Guidelines:

Many reputable medical and educational organizations recognize the importance of the synthetic midurethral sling in the treatment of urinary incontinence in women. According to their website: www.abog.org, the American Board of Obstetrics and Gynecology (ABOG) is "an independent, not-for-profit organization that certifies obstetricians and gynecologists in the United States and Canada." ABOG publishes a "Guide to Learning in Female Pelvic Medicine and Reconstructive Surgery" (FPMRS). According to the latest version, published in 2012, a fellow in FPMRS must be able to Perform and describe the indications, intra and postoperative

complications, and success of the following continence procedures"…. Sling Procedures…. Synthetic- retropubic and Transobturator.

The International Urogynecological Association publishes guidelines regarding training of FPMRS fellows internationally. IUGA's most recent publication on education states that "the trainee should receive experience in the theory, practice, and performance of procedures listed below." The list includes "Sling procedures; retropubic, pubo-vaginal, midurethral and Transobturator." (Drutz JP, IUGA Education Committee. Int Urogynecol J (2010) 21:1445-1453.)

The American College of Obstetricians and Gynecologists have issued a Committee Opinion in June 2014, in conjunction with the American Urogynecological Society. The report describes that 260,000 surgeries for stress urinary incontinence were performed in 2010. Recognized surgical options include synthetic midurethral slings. (ACOG Committee Opinion, Number 603, June 2014.)

Safety of synthetic midurethral slings in the long term

The rate of late complications, pain and erosion with TVT device is very low and the long term data demonstrates that the TVT mesh is biocompatible at long term.

MUS RCTs and Long Term Studies

There are over 150 RCTs with TVT and TVT-O establishing their efficacy and safety. There are numerous long term studies with both TVT and TVT-O which also establish their efficacy, with objective and subjective cure rates typically in the 80-95% range, and safety as a minimally invasive device. (Nilsson 2008, 11 year TVT study; Liapis 2008, 7 year TVT study; Olsson 2010, 11 ½ year TVT study; Liapis 2010, 4 year TVT-O study; Angioli 2010, 5 year TVT-O study; Groutz 2011, 10 year TVT study; Aigmueller 2011, 10 year TVT study; Groutz 2011, 5 year TVT-O study; Cheng 2012, 5+ year TVT-O study; Heinonen 2012, 10 ½ year TVT study; Serati 2012, 10 year TVT study; Nilsson 2013, 17 year TVT study; Svenningsen 2013, 10 years and 9 month TVT study; Serati 2013, 5 year TVT-O study; Laurikainen 2014, 5 year TVT-O RCT; Athanasiou 2014, 7.5 year TVT-O study). To put this into perspective, data on the open Burch at 14 years in 190 women revealed significant urinary incontinence in 56% of patients and just 19% of women remained completely dry. (Kjolhede 2005)

Tomaselli et al published a meta-analysis reviewing the long-term outcomes of retropubic MUS (RP-MUS) and mid-term outcomes of obturator slings (TO-MUS). (Tomaselli 2015) The review included 39 studies (11 RCT's and 38 non-randomized studies) covering 6406 women. The conclusions were that both RP-MUS and TO-MUS have high objective and subjective cure rates in the long and medium term. As far as safety, vaginal erosions (extrusions) were reported at 2.1% and 2.7% for RP-MUS and TO-MUS. Persistent or pain lasting beyond the immediate post op period was reported in only 13 out of 3,974 women (0.3%) with RP-MUS and 30 of 2,432 (1.2%) with TO-MUS. Chronic voiding dysfunction was reported for 55 RP-MUS and 30 TO-MUS patients, without mention of preexisting voiding problems. Recall that the only complications unique to synthetic slings are erosions and

extrusions. The authors concluded that both retropubic and obturator midurethral slings have high efficacy associated with a high safety profile and a low risk of complications which are "seldom severe".

The Svenningsen 2013 TVT registry reported that over a 10 year period, 3 mesh exposures were diagnosed and surgically managed while 1 asymptomatic case was discovered resulting in total number of 4 (0.8%) exposures over a decade. Serati reported on 10 year follow up for women having undergone a TVT for SUI. No patient in this series required sling release during the decade long observation. No significant POP, vaginal, bladder, or urethral erosion, or de novo dyspareunia were noted in the remaining 58 patients."(Serati 2012) In the Laurikanian 5 year RCT of TVT versus TVTO there were no tape problems in the TVT arm and it was noted that "No woman had any sign of tissue reaction, erosion, or tape protrusion at their 5-yr follow-up." (Laurkianian 2014)

In the Heinonen 2012 10.5 year TVT study only 1 patient (0.8%) had a tape erosion in bladder and two patients with retention and pain (1.6%) had the tape cut without any further problems. This is consistent with my clinical experience and other literature demonstrating that tape release is an effective way of addressing later retention with many patients having no problems and remain continent with low rates of recurrent incontinence in women who require a sling release. In the Aigmueller 2011 10 year TVT study two patients had reoperations in the interim caused by bladder or urethral erosion (Table 2 [n=141, 2/141 = 1.4%]). At the time of long term follow-up, there was 1 minor vaginal erosion detected that was treated conservatively (1/117 = 0.8%), but no additional erosion was detected during

cystourethroscopy. This is also consistent with my experience that many TVT mesh exposures can be treated conservatively. Surgery if necessary can be quickly be done in office usually with simple excision and closure. The minority of patients require a return to the operating room. These data area also consistent with the Nilsson 11 and 17 year TVT studies that reported no late term tape complications and one asymptomatic exposure in a patient who was continent and happy with her TVT.

In the Olsson 2010 10 year TVT study it was observed that "One patient had a defect in the healing of the net two months post-operatively [1/124 = 0.8%]" This is a simple wound complication as can occur with any incision line as are many early term reported sling vaginal exposures. The authors also "did not observe any late tape rejection." Per-operative bleeding (>100 ml) occurred in 2.7% (4/124), bladder perforation in 2.7% (4/124) and urethral injury in 1.4% (2/124), and at long term follow up none of these patients with previous complications had any voiding difficulties. These complications are treatable. For example, bladder perforation is recognized during the peri-operative cystoscopy. The trocars are repositioned without long term clinically significant effect.

In the Liapis 2008 7 year TVT study there was one case of TVT tape erosion which developed at 29 months postoperatively (1/65 = 1.5%). The exposure was treated by simply cutting the TVT tape edges which were projecting through the vaginal mucosa and the patient remained continent. The rest of the patients had no evidence of tape erosion at 7-year follow-up." In the Novara 2008 metaanalysis Table 6 includes over 30 studies specific to the TVTR

device with at least 2 years follow up and the rate of vaginal erosion was 1.1%. The rate of reoperation was also very low at 3.2%.

Similar low rates of reoperation in other trials more recently reported. Nguyen 2012 reported 2.2% of the patients had reoperation consisting of 1.3% for voiding dysfunction or urinary retention, 0.8% for vaginal mesh erosion, 0.08% for urethral erosion, and 0.04% for pain (1/3,747). Jonsson Funk 2013 reported a 9 year risk of sling revision/removal of 3.7%. The SGS systematic review and metaanalysis by Schimpf 2014 reported a 1.9% rate of return to the OR for erosion and 1.2% return to OR for urinary retention. Unger 2015 reported a 2.7% rate of reoperation overall, with pain and dyspareunia being a reason for removal in only 7 of 3,307 patients (0.2%). Most recently, Welk 2015 reported a 2.2% operative intervention rate for mesh complications and a 3.3% 10 year cumulative rate of complications.

Heinonen also observed that "63% of patients with mixed urinary incontinence before surgery indicated complete cure, whereas the rate of de novo urgency was 20%. This percentage seems stable over time. Olsson et al reported a de novo urgency rate of 21% 11 years after TVT. In large epidemiologic studies, the prevalence of OAB symptoms in postmenopausal women, according to the ICS definition, varies between 20% and 40%, increasing with age. This is quite consistent with the prevalence in our study population at the time of follow-up, so that we conclude that TVT does not appear to raise the risk for OAB symptoms significantly." I share in this opinion. I counsel my patients that in our practice, the average age of a woman undergoing a sling is 52 years old. In the following decade, many women initiate medication for hypertension, gain weight, become diabetic, develop pelvic

arthritis, lower back disc disease, begin medications with a side effect of constipation. These factors along with an aging bladder contribute to development of OAB symptoms whether or not a woman has had a sling surgery.

The consistency in the TVT and TVT-O data are compelling and show it is safe, effective and an optimal choice for SUI treatment. No other device or SUI surgery has nearly the amount or duration of data as observed in the Ford 2015 Cochrane Review which included 81 trials that evaluated 12,113 women as well as the Tommaselli 2015 systematic review and metaanalysis of medium and long term data. Both showed a 2.1% rate of mesh exposure for TVT similar to the data reported above, which was not significantly different from the 2.4% reported in the Ford 2015 Cochrane Review and 2.7% reported in the Tommaselli 2015 systematic review and metaanalysis for TO-MUS. These long term results decry the idea that complications increase over time after a synthetic midurethral sling.

The above studies reported low rates of chronic pain, and Cochrane review concluded that mid-urethral sling operations, and in particular the TVT which has the most data, "have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI." They also concluded that the "reported occurrence of

problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of these tapes."

I share in these opinions based on these and other data as set forth in my report. For example the AUA's 2012 updated systematic review and SUI guidelines and the SGS 2014 systematic review and treatment recommendations show lower rates of pain, sexual dysfunction and dyspareunia for TVT than the autologous pubovaginal sling and the Burch.

These data support my opinion that the TVT and TVT-O are safe and effective devices and have excellent efficacy and durability. The TVT and TVT-O are the procedure of choice for women as it provides a well-known and established treatment for SUI, making it desirable and useful to surgeons and patients. It is minimally invasive and safer as compared to the Burch and autologous pubovaginal slings as shown in the data of several metaanalyses, systematic reviews and guidelines.

Unlike the multi-filament mesh like Ultrapro, which was tested and failed as a sling in cadaver labs, was rejected by two-thirds of surgeons as a sling concept, and has not been studied like TVT or TVT-O with the volume of RCTs, metaanalyses, systematic reviews and other long term follow up, the 1.1 cm strip of macroporous, monofilament Prolene polypropylene mesh used in TVT and TVT-O is the most suitable for use in treating SUI. Early studies by Petros, Ulmsten and Falconer finding that other materials like Gore-tex, Mersilene and Marlex are not tolerated while Prolene polypropylene is optimal are consistent with these data. The recent Cochrane review (Ford 2015) is consistent with these data as it shows that:

- Type 1 macroporous, monofilament mesh such as the Prolene polypropylene mesh used in the TVT has the highest biocompatibility with the least propensity for infection.
- Pore size affects the inflammatory response and resultant connective tissue formation within and into the mesh, and the rearrangement of materials such as collagen within the mesh structure.
- Macroporous meshes (pore size in excess of 75 μm) easily allow macrophages, leukocytes, fibroblasts, blood vessels and collagen to transverse the pores: thus macroporous meshes promote tissue host ingrowth with resultant biocompatibility and low risk of infection (Amid 1997).
- Monofilament tapes are widely available and now predominate in current clinical practice.

These data are also inconsistent with claims of mesh degradation and inferiority of mechanically cut mesh by Plaintiffs' experts. I have used the TVT for about 17 years as well as the TVT-O and the more recent TVT Abbrevo and TVT Exact devices, and have noticed no clinical difference between mechanical and laser cut mesh nor does the medical literature support a clinically significant difference. I have reviewed photographs of the mesh being stretched 50% and it is my opinion that this is a laboratory scenario, as the mesh is not similarly stretched during implantation. The sheath reduces friction and carries the load as the sling passes through the retropubic space and the sling is placed loosely with space under the urethra with a blunt instrument as set forth in the IFU and Professional Education materials. Moreover, even if random particles got into the vagina and retropubic space, they would cause no clinical effect. The materials are made of the same Prolene as Prolene sutures, which are

used in retropubic suspension procedures like the Burch colposuspension, in the placement of pubovaginal slings, and in various prolapse procedures like the vault suspensions. These Prolene sutures also have decades of use outside SUI and prolapse procedures and are well tolerated and durable. These data and other are also inconsistent with claims of the TVT mesh causing malignant transformation or cancer. (King et al. 2014; King & Goldman 2014; Moalli et al. 2014; AUGS-SUFU 2014 FAQs by Providers on Mid-urethral Slings for SUI; Linder et al. 2016)

The multitude of worldwide long term data, the majority being studies performed by Urogynecologic and Urologic surgeons independently of the manufacturers, refute Plaintiffs' experts' theories. Both prolapse and hernia literature and documents, as well as animal studies, that are cited by the Plaintiffs' experts have no bearing on how the TVT or TVT-O operates and are not relevant. An abundance of Level 1 data, systematic reviews and SUI guidelines for the TVT and TVT-O demonstrate that MUS are safe and effective. The reliable scientific data show that complications are infrequent and manageable and reoperation rates are very low. Significant long term pain and dyspareunia are very rare with TVT and TVT-O. Thus, plaintiffs' espoused theories regarding the weight, pore size, mechanical versus laser cut, inflammation, cytotoxicity, malignant transformation and cancer, and degradation are not scientifically reliable and contrary to the clinical data.

<u>TVT & TVT-O IFU/ patient brochure and professional education:</u>

I have been preceptor for MUS professional education for Ethicon. The professional education curriculum and availability of preceptors and learning opportunities were well

planned, thorough and went well beyond industry norms. Surgery and potential risks were discussed. During these activities I did didactic lectures, instructed in cadaver labs, proctored physicians who observed my cases in my operating room, observed surgeons on their first cases in their operating rooms and taught in the IFU. I believe that the IFU is adequate in providing information concerning the potential risks of the TVT and TVT-O to the intended users, namely pelvic floor surgeons who perform SUI surgery. The IFU further states that surgeons should undergo the professional education, which supplements the IFU. It is not a comprehensive treatise on pelvic floor surgery. That is what our education, training, experience and continuing medical education provide to us as surgeons. As pelvic floor surgeons, we know the potential risks of SUI surgery and the only unique risk with the MUS is mesh exposure, although as noted earlier wound complications and suture erosions occur with non-mesh SUI surgeries. The basic elemental risks with SUI surgery are taught to us during training, learned by reading the medical literature and practicing clinically, discussed in professional capacities such at meetings, and studied in connection with professional medical education and our certification process.

I have also reviewed the patient brochures and it is my opinion that they adequately convey basic information to the lay person and recommend that the patient discuss her condition and options with her surgeon. The brochure is not and does not supplant the patient-surgeon relationship and consenting. Only we as surgeons know what a particular patient's background, history, presentation, bother and options are in the exercise of our medical judgment, and our discussion of the potential benefits and risks of options comes from our education, training, experience, our discussions with colleagues, attendance at professional meetings and the medical literature.

Urge Incontinence

Urge incontinence is also a well-known risk to surgeons performing prolapse and stress incontinence surgery. In 1991, Beck reported his experience gathered over 25 years performing anterior repairs for stress incontinence. 3/519 patient required transfusion. Interestingly, the new onset of detrusor instability after surgery was 6%.

For many years, prior to the introduction and acceptance of the tension free vaginal tape, the Burch urethropexy was the primary incontinence surgery performed. In 1979, Cardozo published on the incidence of new onset of Detrusor Instability (now called detrusor Overactivity) in women who underwent a Burch colposuspension. The study involved 92 women who were found to have Genuine Stress Incontinence on urodynamics testing and otherwise normal bladder function. As part of the study, the women underwent urodynamics in the postoperative period; 17/92 (18.5%) were found to have new onset DI.

Soon after, Dr. Chaikin, along with his colleague, Dr. Blaivas presented long term results of women undergoing fascial Pubovaginal sling. Two hundred fifty-one women who had undergone Pubovaginal sling for stress incontinence, and who had at least one year follow up were assessed by a 3rd party. Complications included: denovo or persistent urge incontinence and permanent urinary retention.

The TVT IFU adequately warns of the risk of urge incontinence by warning surgeons that, as with other procedures, detrusor instability can occur. (TVT IFU)

Pelvic Floor Hypertonicity Disorder

Dr. Butrick, a leading expert on pelvic pain and Urogynecology, published 2 chapters on Pelvic Floor Hypertonic Disorder in Obstetrics and Gynecology Clinics of North America. Risk factors for Pelvic pain of a myofascial etiology are: recurrent urinary tract infection, ureteral reflux, vulvar pain and constipation. Further, he reports that pelvic floor dysfunctions can be learned behaviors, because of holding patterns and gives the example of nurses who spend years holding their urine while working their shift. Further, direct injury to the levator muscle complex affects pelvic pain and dyspareunia. Examples of direct injury include traumatic vaginal delivery and surgery which involves fixation to muscle sites, such as a posterior colporrhaphy in which the levator muscles are plicated.

While women complaining of pelvic pain may believe that the source of pain is the uterus or ovaries, frequently the source is myofascial involving the muscles, connective tissue (ligaments) and or nerve supply in the region. (Spitznagle 2014) according to Spitznagle, a women's health physical therapist, recognized treatments include: soft-tissue mobilization, biofeedback, electrical stimulation, correction of movement impairments with therapeutic exercise and activities, and dry needling. Trigger point injections and use of vaginally administered steroid, muscle relaxants and anesthetics are also effective.

Dyspareunia

Dyspareunia is also a recognized risk to surgeons performing prolapse and stress incontinence surgery. Pauls et al in 2007, presented results of a prospective study evaluating the sexual function of currently sexually active women before and after vaginal surgery with or without a concomitant anti-incontinence procedure. Forty-nine of 50 women completed assessment at 6 months post op. They found that the most bothersome barrier to sexual activity before prolapse repair was vaginal bulging, but post operatively it was vaginal pain. An incontinence procedure had no effect on the results. (Pauls 2007)

Dyspareunia rate increased from 43% to 57% after posterior repair, while the no PR group decreased from 53% to 28%. (Komesu 2007)

Weber et al reported on 165 women who had at least 6 month follow up after surgery for prolapse, incontinence or both. Dyspareunia increased from 8% pre-op to 19% post-operatively. In further comparison, dyspareunia remained after surgery in one women, appeared denovo in 14 and resolved in 5. (p= 0.04). (Weber 2000) The anatomic findings did not necessarily correlate to the complaints of painful intercourse. Thus, the literature is replete with studies discussing the risk of dyspareunia with vaginal surgery, especially prolapse repair. Pain, dyspareunia and new onset OAB are risks well known by any surgeon performing incontinence surgery and/ or prolapse repairs. Significant long term pain and dyspareunia are very rare with TVT and TVT-O.

My Summary

Based on my training, review of the literature and clinical experience, among other things, I am in agreement with the statements, analyses and guidelines reviewed above. Synthetic midurethral slings are clearly recognized as first line, gold standard and standard of care both in the United States and abroad.

I practiced medicine before synthetic midurethral slings became available. Earlier in my career, only restoration of anatomy was used, such as paravaginal repair, and compensatory defects such as Kelly plication and Burch were used to treat incontinence. I have performed many bladder neck slings. When synthetic midurethral slings were first made available, I initially used them cautiously, using MUS if only vaginal surgery was planned, and then even if abdominal hysterectomy and abdominal repair of prolapse required, I would perform a TVT vaginally for incontinence. The reason is that slings (MUS) have the highest cure of incontinence, the most durable cure of incontinence, the least complications and are very unlikely to result in non-treatable adverse symptoms. When I reflect on women on whom I performed a bladder neck sling or a Burch, or an MMK, who ended up with permanent, non-reversible urgency, painful urination, incomplete bladder emptying with resultant chronic bladder infections, or chronic use of CISC, I am confident that I will never go back to the "old days."

TVTs have been revolutionary in advancing the treatment of women with SUI. Further, because Burch's and slings involved significant morbidity, in years past, women would be advised to hold off on surgical treatment until incontinence was quite severe. Because MUS are minimally invasive, with short recovery times, and low risk of serious complications, most

women can opt for surgical treatment of SUI as first line therapy with markedly improved quality of life. Further, if a woman develops incomplete bladder emptying after a midurethral sling, this problem is reversible by performing a sling release. If partial or complete urinary retention occurred after a Burch or a fascial pubovesical sling, these adverse events might resolve with time, but are largely not reversible with medications nor urethrolysis. As a busy clinician, I also realize that there is often a vast difference between in vitro data (laboratory findings) and in vivo performance. Since the real life experience of my patients and the patients represented in study after study strongly demonstrate the biocompatibility of polypropylene slings. Thus, plaintiffs' espoused theories regarding the weight, pore size, mechanical versus laser cut, inflammation, cytotoxicity, malignant transformation and cancer, and degradation are not scientifically reliable and contrary to the clinical data.

In conclusion:

I completely agree with AUGS and SUFU that-

- The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence.
- The procedure is safe, effective, and has improved the quality of life for millions of women.
- This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years

I continue to offer synthetic midurethral slings, and in particular TVT products to my patients without hesitation.

Denise M. Elser, M.D.